Melanoma survival in the United States, 1992 to 2005

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Abstract

Background—Population-based data on melanoma survival are important for understanding the impact of demographic and clinical factors on prognosis.

Objective—We describe melanoma survival by age, sex, race/ethnicity, stage, depth, histology, and site.

Methods—Using Surveillance, Epidemiology, and End Results data, we calculated unadjusted cause-specific survival up to 10 years from diagnosis for 68,495 first primary cases of melanoma diagnosed from 1992 to 2005. Cox multivariate analysis was performed for 5-year survival. Data from 1992 to 2001 were divided into 3 time periods to compare stage distribution and differences in stage-specific 5-year survival over time.

Results—Melanomas that had metastasized (distant stage) or were thicker than 4.00 mm had a poor prognosis (5-year survival: 15.7% and 56.6%). The 5-year survival for men was 86.8% and for persons given the diagnosis at age 65 years or older was 83.2%, varying by stage at diagnosis. Scalp/neck melanoma had lower 5-year survival (82.6%) than other anatomic sites; unspecified/overlapping lesions had the least favorable prognosis (41.5%). Nodular and acral lentiginous melanomas had the poorest 5-year survival among histologic subtypes (69.4% and 81.2%, respectively). Survival differences by race/ethnicity were observed in the unadjusted survival, but nonsignificant in the multivariate analysis. Overall 5-year melanoma survival increased from 87.7% to 90.1% for melanomas diagnosed in 1992 through 1995 compared with 1999 through 2001, and this change was not clearly associated with a shift toward localized diagnosis.

Limitations—Prognostic factors included in revised melanoma staging guidelines were not available for all study years and were not examined.

Conclusions—Poorer survival from melanoma was observed among those given the diagnosis at late stage and older age. Improvements in survival over time have been minimal. Although newly available therapies may impact survival, prevention and early detection are relevant to melanoma-specific survival.

Keywords

anatomic sites; cancer registry; histology; melanoma; survival

More than 50,000 people are given the diagnosis of melanoma in the United States every year, according to the US Cancer Statistics report.[1] In addition to the stage at diagnosis, previous studies have shown other factors are related to prognosis such as histology, location on body, and socioeconomic status (SES).[2-5] In this study, we used the data from population-based cancer registries to describe melanoma survival by demographic and clinical factors.

METHODS

We analyzed data from the 13 registries that participate in the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) program (Atlanta, GA; Connecticut; Detroit, MI; Hawaii; Iowa; New Mexico; San Francisco-Oakland, CA; Seattle-Puget Sound, WA; Utah; Los Angeles, CA; San Jose-Monterey, CA; rural Georgia; and the Alaska Native Tumor Registry). The coverage of these SEER-13 registries represented 14% of the US population and met uniform data standards for cancer registration.[6]

We identified 133,386 cases of melanoma diagnosed between 1992 and 2005 at age 15 years or older and reported to a SEER-13 registry. We excluded 37,160 in situ melanoma cases (27.9%); 26,282 melanoma cases that were not the first cancer diagnosed (19.7%); 145 cases found by death certificate only or autopsy; 275 cases not microscopically confirmed; 318 cases with an unknown cause of death; 88 patients with unknown age; and 623 patients who had no survival time. Our final study population included 68,495 first primary invasive melanoma cases diagnosed in years 1992 to 2005 and followed up through 2006 to ensure at least 12 months of complete follow-up. Melanoma cases were identified by International Classification of Diseases for Oncology, Third Edition morphology codes (C440-C449)[7] and categorized by histologic subtype as superficial spreading, lentigo maligna, acral lentiginous, nodular, not otherwise specified, and other.[8] We chose not to collapse the histologic category "not otherwise specified" with "other" because the survival patterns for these two subtypes were different. A revised staging system for melanoma was introduced in the sixth edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual and implemented into cancer registries in 2003.[9] To ensure consistency in staging across all study years, we used SEER historic stage, which provides consistent definitions over time (as opposed to AJCC staging, which is more commonly used in the clinical settings).[10] SEER historic stages were localized (confined to primary site), regional (spread to regional lymph nodes), distant (cancer had metastasized), and unknown (unstaged). Depth of melanoma was classified as less than or equal to 1 mm, 1.01 to 2.00 mm, 2.01 to 4.00

mm, and greater than 4.00 mm. Anatomic sites were classified as face/ears (C440-C443), scalp and neck (C444), trunk (C445), extremities (C446-447), and not otherwise specified/ overlapping codes (C448-C449).[7] Scalp and neck melanomas have been shown to have poorer survival than melanomas on the face, ear, and other anatomic sites,[3] thus we analyzed them separately. Information on race and ethnicity was obtained from medical records by tumor registrars who reported melanoma to the SEER program.[6] Identification of cases having Hispanic ethnicity was enhanced with the North American Association of Central Cancer Registries Hispanic Identification Algorithm.[11] The availability and quality of variables on receipt of surgery, sentinel lymph node biopsy (SLNB), and radiation were limited, especially in the earlier years, and therefore not included in this analysis.

Analysis

Our main outcome of interest was survival time after a diagnosis of melanoma as the primary cancer. The cause of death information was from death certificates. We present cause-specific survival (eg, melanoma-specific survival [MSS]). For the unadjusted analyses, we used the Kaplan-Meier method to calculate MSS by gender, age at diagnosis, race, Hispanic ethnicity, stage and depth at diagnosis, anatomic site, and histologic subtype. To examine temporal trends in survival, we stratified cases into 3 time periods (1992-1995, 1996-1998, and 1999-2001). For this analysis of survival time by time period and stage, we excluded cases diagnosed after 2001 to have a full 5 years of follow-up. We used the Z-test to examine any differences in 5-year survival between the earliest and most recent time period and χ^2 to test for any significant change in the proportion of cases diagnosed at the local, regional, distant, and unknown stage (eg, stage distribution).

We explored whether survival differences can be explained by sociodemographic and clinical characteristics by performing a multivariate analysis for MSS using Cox regression modeling. Because of missing information on race/ethnicity, stage at diagnosis, and depth, this multivariate analysis was based on 56,886 study cases. We restricted the follow-up time in the Cox model to a 5-year follow-up period. We assessed the Cox proportional hazards assumption for each covariate by graphical examination of the log of the negative log survival curves versus time and by the Schoenfeld residual correlation test. Variables for histologic subtype and anatomic site were both found to violate the Cox proportional hazards assumption. Thus, the final Cox model was stratified on histologic subtype and anatomic site and included sex, age at diagnosis, race/ethnicity, stage at diagnosis, and depth.[12,13] Hazard ratios (HR) and corresponding 95% confidence intervals (CI) were estimated to determine statistical significance. All the analyses were performed using SEER*Stat, Version 6.6 (IMS Inc, Silver Springs, MD) and SAS, Version 9.2 (SAS Institute, Cary, NC).

RESULTS

This study included 68,495 invasive melanoma cases diagnosed from 1992 to 2005 in the 13 SEER registries. Table I shows the distribution of melanoma incidence by demographic and clinical characteristics and 1-, 5-, and 10-year MSS. Figs 1 and 2 show Kaplan-Meier cause-specific survival curves. Overall, the 1-year MSS was 96.9%. The 5- and 10-year MSS were

89.2% and 85.1%. The MSS for males and females was 96.3% and 97.7% at year 1 and 86.8% and 92.0% at year 5, respectively. Age at diagnosis impacted survival. Men and women given the diagnosis at age 65 years and older had a lower 5-year survival than those at age 40 to 64 years and 15-39 years (83.2% vs 90.6% and 94.4%) (Table I). As time from diagnosis increased, so did the differences between the MSS of the oldest and younger age groups (Fig 1). The 10-year MSS was 77.0% for cases diagnosed at age 65 years, which was lower than 86.7% and 91.9% for the two younger age categories. We analyzed MSS by age and stage at diagnosis and found that the difference between the youngest (15-39 years) and oldest (65 years) age group was more pronounced for regional stage melanomas (73.5% vs 58.2%) than localized stage (98.0% vs 92.3%) (data not shown). Whites accounted for 95.2% of the study population and had a favorable prognosis at diagnosis (96.9% 1-year and 89.0% 5-year MSS) compared with blacks (72.2% 5-year MSS) and Asian/Pacific Islanders (79.2% 5-year MSS). Ethnicity also impacted survival. Non-Hispanic whites had a higher 5-year survival than Hispanic whites (89.2% vs 82.9%). Melanoma diagnosed at the localized stage had a 99.7% 1-year MSS, but despite early detection there were still deaths attributable to melanoma at the localized stage (10-year MSS 92.1%). In contrast, diagnoses at a distant stage had poor prognoses (1-year MSS 41.3%). For regional and distant stage melanomas, MSS decreased rapidly from year 1 to year 3 and then stabilized from year 5 to year 10 (Fig 2, *A*). Given that depth of melanoma is a major determinant of stage of diagnosis, as expected, lesions less than 1.00 mm had a 5-year MSS of 97.4% whereas the 5-year MSS for lesions that were 2.01 to 4.00 mm was 72.7% and, for lesions with a depth greater than 4.00 mm, MSS was 56.6% (Fig 2, *B*). Two histologic subtypes with favorable prognosis were superficial spreading and lentigo maligna. For both, MSS exceeded 99% at year 1, 95% MSS at year 5, and remain over 92% at year 10 (Fig 2, *C*). In contrast, the 1-, 5-, and 10-year MSS of nodular and acral lentiginous melanoma were substantially different. Survival by anatomic site was similar for melanoma diagnosed on the face/ears, trunk, and extremities (5-year MSS 90.2%, 91.2%, 92.5%) but less for melanoma on the scalp and neck (5-year MSS 82.6%, 10-year MSS 75.6%) and unspecified and overlapping lesions (5-year MSS 41.5%) (Fig 2, *D*).

A modest increase in the overall 5-year cause-specific survival for melanoma was observed between the time periods of 1992 to 1995 (87.7% [95% CI 87.1-88.2]) and 1999 to 2001 (90.1% [95% CI 89.6-90.5]) (Table II). Comparing these two time periods, there was a decrease in the proportion of unstaged cases from 5.9% to 2.1% of overall cases (*P* < .001). Among the cases that were staged, compared with cases diagnosed in 1992 through 1995, the proportion of localized cases decreased in the most recent time period of 1999 to 2001, whereas the proportion of cases diagnosed at the regional stage increased, and the change in proportion diagnosed at the distant stage was very small (*P*<.001 for overall change in distribution). Patients given the diagnosis at the localized and regional stages from 1999 to 2001 had significantly increased 5-year survival compared with patients given the diagnosis of same-stage cancer from 1992 to 1995. For melanoma diagnosed at a distant stage, there was a slight, but not significant, increase in 5-year MSS from the earliest to latest diagnostic time period.

After controlling for demographic and clinical factors through multivariate analysis, we found sex and age remained significantly associated with 5-year survival (Table III). The

risk of death for females was lower than for males (HR 0.76 [0.71-0.81]), as were the two younger age groupings (HR 0.66 [0.62-0.71] for ages 40-64 years and HR 0.49 [0.44-0.54] for ages 15-39 years) compared with those older than 65 years. Racial/ethnic differences in survival were attenuated in our multivariate model. The risk of melanoma death for blacks was over one-third higher than for non-Hispanic whites, but did not reach statistical significance (HR 1.33 [0.98-1.78]). The survival differences by Hispanic ethnicity (limited to cases of white race) also lost significance in the multivariate analysis (HR 1.06 [0.92-1.24]). We found the stage at diagnosis and depth of melanoma to be important factors related to 5-year survival.

DISCUSSION

Our study results are consistent with earlier reports that stage at diagnosis and depth are significant factors related to MSS.[9] Although depth is one factor that determines stage, the correlation between them was modest (21%), therefore, we kept both depth and stage in the model. Sex and age also remained significant prognostic factors in the adjusted analysis, with worse survival for men and those who were elderly at diagnosis. The difference in survival by age may be related to comorbidities, which could not be directly accounted using SEER data. Although we observed survival differences by race and ethnicity (for whites) in the unadjusted analysis, the association of race and ethnicity with survival was attenuated in the multivariate analysis.

Gender difference in melanoma survival have been reported in other studies.[9,14-16] Although this observation is not well understood, previously published findings have suggested that older patients are given the diagnosis at later stages as a result of less screening; men are given the diagnosis of more nodular melanoma, which has a poorer prognosis; and that women undergo more screening and have melanomas in more favorable anatomic locations.[10,15,17,18] Our multivariate analysis results showed that even adjusting for stage, the risk of death from melanoma was still higher for men than for women. Regarding race, the adjusted risk of death for blacks was higher than for non-Hispanic whites, but not statistically significant. This observation supports that there are racial differences in sex, age, and clinical factors of melanoma at diagnosis, which in turn impact survival. Previous studies have shown that blacks are disproportionately affected by acral lentiginous melanoma, a histologic subtype with worse survival than overall melanoma, likely because of acral lentiginous melanoma being diagnosed at later stages with thicker lesions.[2,19] After accounting for stage, depth, and histologic subtype, we found survival differences for blacks compared with whites were less than in previously published work by Zell et al.[5] Two major differences, however, were that the analysis of Zell et al[5] used only California Cancer Registry data with 127 cases of melanoma among blacks, whereas our study used national SEER-13 data that included over twice the number of blacks; and, unlike the analysis of Zell et al,[5] we did not adjust for SES and treatment. SES has been related to melanoma survival with increased survival for nonwhites and elderly persons with higher SES.[4,5]

We observed small improvements in survival at the localized and regional stage. A factor that could explain these observations and may have contributed to an increase in survival at these earlier stages is the adoption of SLNB around the year 2000, a technique that more

precisely identifies potentially affected lymph nodes.[20] Using SLNB, some melanoma cases that may have been classified as localized are identified as regional because of the increased specificity of the diagnostic workup. As a result of this upstaging, the survival at the regional disease improves because of the addition of cases that would have otherwise been classified as localized, and survival at the localized stage also improves because of the identification and classification of more disseminated disease as regional stage.[9,21] The impact of SLNB on overall survival is a topic of much debate in the current literature because the early removal of lymph nodes with micrometastatic disease has not been shown to improve overall survival, and there have been no randomized trials that have shown that early surgical removal of affected nodes improves overall survival compared with delaying removal of nodes until they are clinically palpable.[22,23]

We showed a small improvement in overall 5-year survival from the early 1990s to the period around the year 2000. During this time we found that more cases were being staged; however, we did not observe a dramatic shift toward melanoma being diagnosed at earlier stages as might be expected from increased screening for melanoma. In fact, among the melanoma cases that were staged, from the earliest to most recent time period, the percentage of all melanomas diagnosed at the localized stage decreased and the percentage of all melanomas diagnosed at the regional stage increased. Jemal et al[24] showed that the incidence rates from 1992 to 2006 increased for all tumor depths, but did not take into account nodal involvement, metastasis, or other criteria that determine stage. Further exploration of how the revised staging systems impact the relative percentages of melanoma diagnosed at the localized versus regional stage warrants further study.

Our cause-specific analysis focused on melanoma as the underlying cause of death and did not include death from all other causes. The validity of MSS depends on the quality of recorded cause of death.[21] Understanding this, we believed that using MSS was justified for our study because of the high quality of SEER data, and because ascertaining death from melanoma is not as challenging as other diseases as a result of ease of obtaining diagnosis through biopsy, and because of the tendency of disseminated disease to metastasize and be detected. Another approach we could have used is "relative survival," which compares the observed survival of those given the diagnosis of melanoma with a comparable population without melanoma, thus bypassing the need for cause for death because of the focus on excess mortality among those with melanoma.[21] We chose not to show relative survival because our preliminary analyses using both cause-specific and relative survival were similar (data not shown) and because there were no life tables available for racial and ethnic groups besides black and white. "Period survival" is an approach that captures improvements in survival to provide better estimates of long-term survival for more recently diagnosed cancer.[25] Given the lack of significant progress in survival shown in our study (Table II), using period survival was unnecessary. A more recent, relevant approach is "conditional survival," which conditions survival upon living to a certain time point, and has been applied to melanoma by Rueth et al[26] to show that 8 years after surgical treatment from melanoma, the survival for high-risk melanoma is similar to low-risk disease.

Strengths of this study were the use of population-based, high-quality SEER data and the large number of melanoma cases, including cases among those who were black or Hispanic.

A limitation is that we were unable to use the complete US Cancer Statistics data set (SEER combined with National Program of Cancer Registries data)[1] because the survival data are not consistently available from all National Program of Cancer Registries. Other limitations include the use of the North American Association of Central Cancer Registries Hispanic Identification Algorithm, which may misclassify Hispanic ethnicity because of the reliance of surname and other demographic variables rather than self-report.[11] We did not account for all factors known to impact survival including treatment, prognostic factors in the revised staging system (nodal involvement, metastasis, and, more recently, mitoses, ulceration, and serum lactate dehydrogenase), SES, and physician specialty or availability as these data are not available in population-based registries.[4,5,14,27,28] Also, we examined survival after diagnosis of the "first and primary" melanoma but did not limit cases to "first and only" melanoma. Thus, our data include people who may have had subsequent cancers, melanoma or otherwise, after a primary diagnosis of melanoma. It is important to be aware that certain medical conditions, such as atypical mole (dysplastic nevi) syndrome or immunosuppression, may predispose one to multiple diagnoses of melanoma and may impact survival.[29-35]

The contrast in melanoma survival by stage at diagnosis offers a compelling reason to support early detection and to support primary prevention through sun protection and avoidance of harmful ultraviolet light; these prevention efforts should be emphasized. Although, routine screening for early detection of lesions is not currently recommended by the US Preventive Services Task Force and Cancer Council Australia,[36-38] early detection through screening should be considered for persons at risk for melanoma. Previous studies have found such screening program to be cost-effective, even if screening is not currently recommended. For instance, Freedberg et al[39] used data from the US population and estimated a cost-effectiveness ratio of $29,170 per year of life saved for a one-time screening of self-selected patients at high-risk with a mean age of 48 years. Further, a study from Australia estimated a cost-effectiveness of annual melanoma screening in Australians aged 50 years or older to be Aust. $12,137 and Aust. $20,877 (US$12,318 and US$21,188) for men and women, respectively.[40]

In conclusion, our study found minimal progress in survival from 1992 to 2005. The relevance of new therapies such as interferon alfa-2b and, more recently, immunotherapy (eg, ipilimumab) on prognosis will be determined in future studies.[20,41] Until then, efforts to reduce melanoma deaths must continue through prevention, screening of persons at high risk, and elimination of disparities that lead to late diagnosis.

Abbreviations used

AJCC	American Joint Committee on Cancer
CI	confidence interval
HR	hazard ratio
MSS	melanoma-specific survival
SEER	Surveillance, Epidemiology, and End Results

SES	socioeconomic status
SLNB	sentinel lymph node biopsy

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CAPSULE SUMMARY

- Cancer registry data were used to calculate cause-specific survival up to 10 years from diagnosis for 68,495 first primary cases of melanoma diagnosed from 1992 to 2005.

- Poorer survival from melanoma was observed among those given the diagnosis at late stage and older age.

- Improvements in survival over time have been minimal.

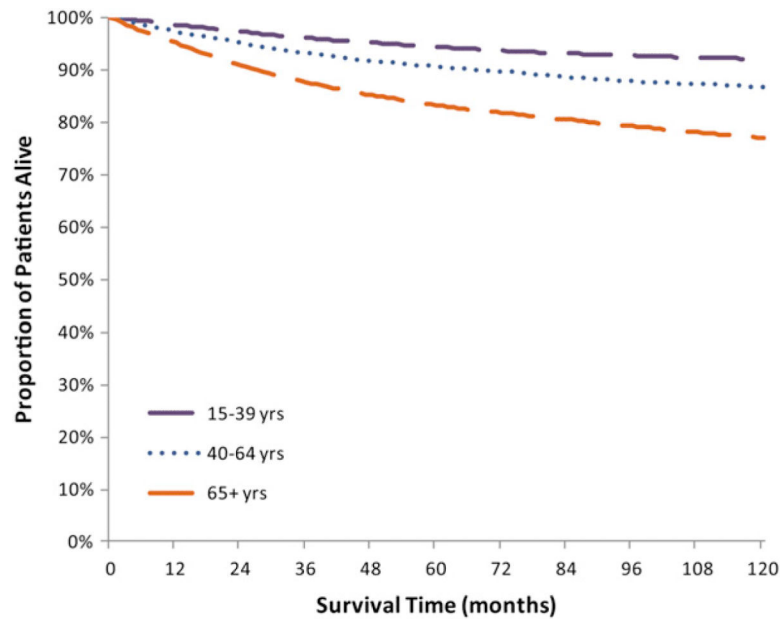**Fig 1.**
Unadjusted Kaplan-Meier melanoma-specific survival curve by age at diagnosis, Surveillance, Epidemiology, and End Results-13, 1992 to 2005.

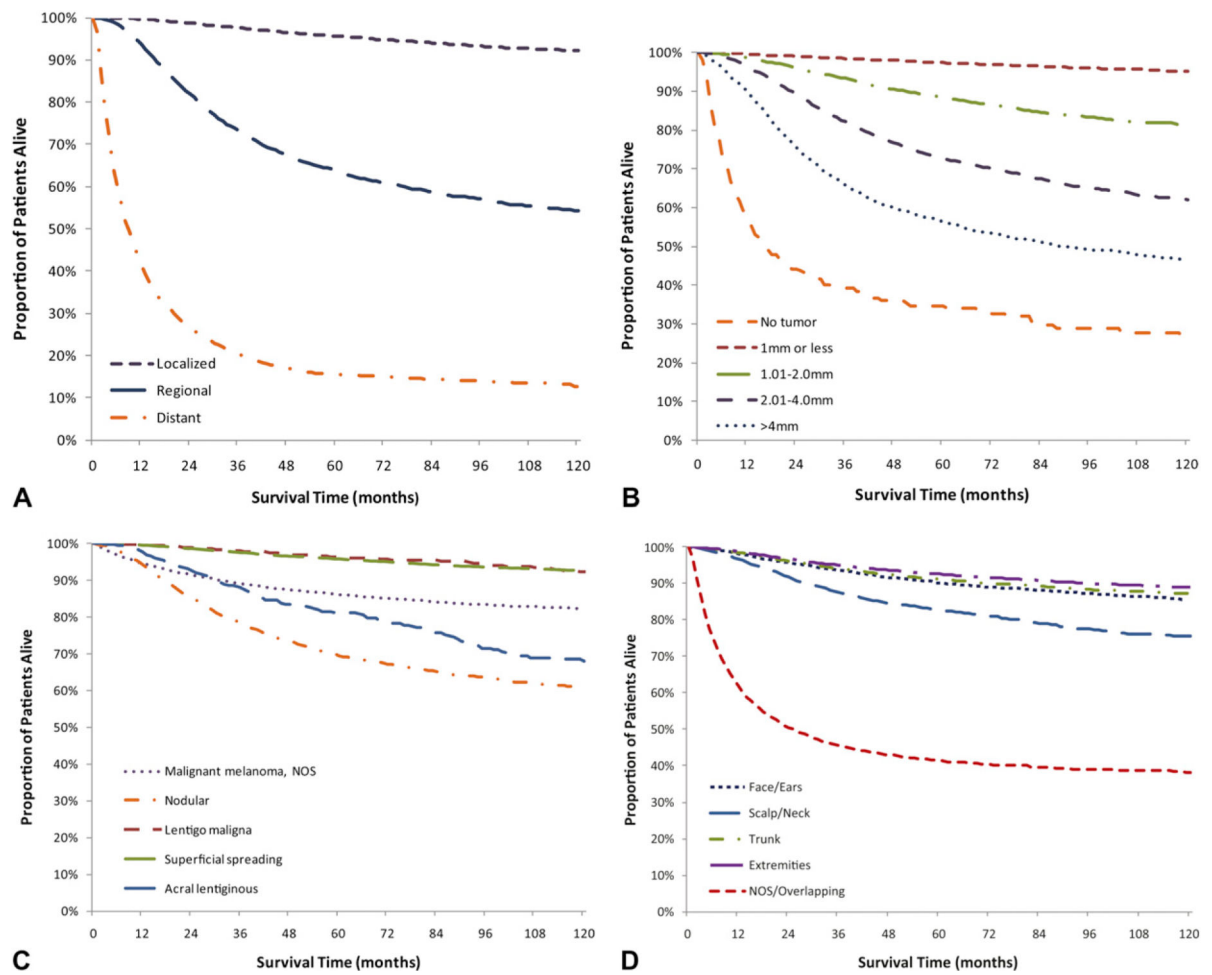**Fig 2.**
Unadjusted Kaplan-Meier melanoma-specific survival curves by stage **(A)**, depth **(B)**, histology **(C)**, and anatomic site **(D)**, Surveillance, Epidemiology, and End Results-13, 1992 to 2005. *NOS*, Not otherwise specified.

Table I

Demographic and clinical characteristics of patients with invasive melanoma, Surveillance, Epidemiology, and End Results-13, 1992 to 2005

Characteristic	No.	Percentage	Melanoma-specific survival, %		
			1-y	5-y	10-y
Overall	68,495		96.9	89.2	85.1
Sociodemographic					
Sex					
Male	37,626	54.9	96.3	86.8	82.0
Female	30,869	45.1	97.7	92.0	88.8
Age at diagnosis, y					
15-39	13,383	19.5	98.6	94.4	91.9
40-64	33,526	48.9	97.4	90.6	86.7
65	21,586	31.5	95.1	83.2	77.0
Race/ethnicity[*]					
White	65,174	95.2	96.9	89.0	84.8
White, non-Hispanic	63,140	92.2	96.9	89.2	85.0
White, Hispanic	2034	3.0	95.1	82.9	79.0
Black	318	0.5	89.5	72.2	68.2
Asian/Pacific Islander	593	0.9	94.4	79.2	71.7
American Indian/Alaskan Native	124	0.2	93.5	79.5	74.6
Other/unknown	2286	3.3	99.8	99.2	98.0
Hispanic	2104	3.1	95.3	83.3	79.5
Clinical					
Stage at diagnosis					
Localized	56,504	82.5	99.7	95.6	92.1
Regional	7365	10.8	93.6	63.7	54.3
Distant	2253	3.3	41.3	15.7	12.8
Unstaged	2373	3.5	93.4	80.3	74.2
Depth, mm					
No mass/tumor found	483	0.7	57.4	34.5	26.4
0.01-1.00	40,935	59.8	99.6	97.4	95.2
1.01-2.00	9520	13.9	98.7	88.4	81.2
2.01-4.00	5190	7.6	96.5	72.7	62.1
>4.00	2955	4.3	91.1	56.6	46.6
Unknown	9412	13.7	87.4	75.4	71.2
Histologic subtype					
Superficial spreading	26,054	38.0	99.5	95.8	92.6
Lentigo maligna	4297	6.3	99.7	96.3	92.4
Acral lentiginous	785	1.1	97.7	81.2	67.9
Nodular	4998	7.3	94.3	69.4	60.8
NOS	29,445	43.0	94.7	86.2	82.2

Characteristic	No.	Percentage	Melanoma-specific survival, %		
			1-y	5-y	10-y
Others	2916	4.3	96.2	83.4	78.1
Anatomic site					
Face/ears	8153	11.9	98.4	90.2	85.5
Scalp/neck	4328	6.3	96.6	82.6	75.6
Trunk	23,293	34.0	98.3	91.2	87.1
Extremities	29,990	43.8	98.7	92.5	88.8
Upper limb/shoulder	16,229	23.7	98.7	93.0	89.5
Lower limb/hip	13,761	20.1	98.6	91.8	88.0
NOS/overlapping	2731	4.0	61.7	41.5	38.2

NOS, not otherwise specified.

[*] Hispanics were not mutually exclusive from race. Whites included both non-Hispanic whites and Hispanic whites.

Table II

Overall melanoma-specific 5-year survival by specified time periods, Surveillance, Epidemiology, and End Results-13, 1992 to 2005

	Period I		Period II		Period III	
	1992-1995		1996-1998		1999-2001	
	N (%)	5-y Survival, % (95% CI)	N (%)	5-y Survival, % (95% CI)	N (%)	5-y Survival, % (95% CI)
Overall	16,262	87.7 (87.1-88.2)	14,286	89.1 (88.5-89.6)	15,604	90.1 (89.6-90.5)
Staged	15,304 (94.1)	88.1 (87.5-88.6)	13,647 (95.5)	88.1 (87.5-88.6)	15,272 (97.9)	90.3 (89.8-90.7)
Unstaged	958 (5.9)	80.9 (78.2-83.3)	639 (4.5)	80.0 (76.6-83.0)	332 (2.1)	79.6 (74.6-83.7)
Staged						
Localized	13,223 (86.4)	94.3 (93.8-94.6)	11,726 (85.9)	95.6 (95.2-96.0)	12,922 (84.6)	96.4 (96.1-96.7)
Regional	1518 (9.9)	59.4 (56.8-62.0)	1468 (10.8)	61.3 (56.8-63.8)	1869 (12.2)	65.5 (63.2-67.7)
Distant	563 (3.7)	14.0 (11.1-17.2)	453 (3.3)	16.4 (13.0-20.2)	481 (3.2)	16.6 (13.0-20.2)

Cases diagnosed after 2001 were excluded to have a full 5 years of follow-up. Percentages may not add to 100 because of rounding.

CI, Confidence interval.

Table III

Cox multivariate analysis of 5-year survival for malignant melanoma, Surveillance, Epidemiology, and End Results-13, 1992 to 2005

Characteristic	Hazard ratio[*] (95% CI)
Sex	
Male	Ref.
Female	0.76 (0.71-0.81)
Age at diagnosis, y	
65	Ref.
40-64	0.66 (0.62-0.71)
15-39	0.49 (0.44-0.54)
Race/ethnicity	
White	
Non-Hispanic	Ref.
Hispanic	1.06 (0.92-1.24)
Black	1.33 (0.98-1.78)
Asian Pacific Islander/American Indian Alaskan Native	0.98 (0.76-1.25)
Stage at diagnosis[†]	
Localized	Ref.
Regional	3.62 (3.35-3.91)
Distant	18.66 (16.54-21.06)
Depth, mm	
1	Ref.
1.01-2.0	2.89 (2.62-3.18)
2.01-4.0	4.69 (4.24-5.02)
>4.0	5.71 (5.10-6.39)
No tumor found	3.03 (1.98-4.64)

CI, Confidence interval.

[*] Survival estimates are from Cox proportional hazards model accounting for histologic subtype, anatomic site, sex, age at diagnosis, race/ethnicity, stage at diagnosis, and depth.

[†] Surveillance, Epidemiology, and End Results (SEER) historic stage based on SEER summary stage 2000.